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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,579	03/22/2002	Lou Franciscus M. H. De Leij	05032-00098	1723

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/009,579

Applicant(s)

DE LEIJ ET AL.

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-9,14,20,21 and 24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-9,14,20,21 and 24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1, 2, 4-9, 14, 20, 21 and 24 are pending in the application.

This Office Action is in response to the Amendment filed on 3/20/07.

#### ***Response to Amendment***

The objection to the specification and claim 5 has been withdrawn.

The rejection of claim 24 under 35 U.S.C. 101 has been withdrawn in light of Applicant's amendment.

The rejection of claims 1, 2, 4-9, 14, 20, 21 and 24 under 35 U.S.C. 112 1<sup>st</sup> paragraph is maintained for reason set forth of the record mailed on 9/20/06 and further discussed below.

#### ***Response to Arguments***

##### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-9, 14, 20, 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants argue that the claims are drawn to a specific sequence having Ets binding sites and Sp-1 binding site at specific positions of the claimed

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sequence, and such binding sites have a specific spatial distribution within the claimed promoter region. Applicants assert that the claimed promoter region having a specific spatial distribution of Ets and Sp-1 binding sites provides a structural feature that correlates with the claimed function of allowing expression of a nucleic acid of interest operably linked to the promoter in a cancer cell in an epithelium selective manner. Applicants assert that the result from the deletion study as shown in Figure 2 illustrates that the 336 base pair region between 442 and 778 does have epithelial specific expression. Applicants thus conclude that the specification provides sufficient description for the claimed invention.

This argument has been fully considered but deemed unpersuasive. The reasons for the written description rejection were discussed in detail in the previous office actions. In response to Applicant's argument, Applicants are invited to first to clarify the relationship between the claimed 356 base pair sequence (3200 to 3556 of SEQ ID NO: 5) and the 336 base pair sequence (between 442 and 778 as discussed in the response). Secondly, assume the 356 base pair sequence comprises the 336 base pair that which comprises elements which has ability to direct epithelial specific expression, whether this 336 fragment can direct epithelial specific expression for a heterologous gene as claimed is unpredictable based solely on the result demonstrated in Figure 2. As Applicants have stated that it is the specific spatial distribution of the putative binding sites is responsible for epithelial expression, the epithelial specific expression may be result from interaction between this 336 fragment and the first 442 base pair of the promoter sequence. Moreover, whether the putative binding site such as Ets and Sp-1 at those specific position actually binds the Ets and Sp-1 is unknown, and whether deletion of such putative binding sites would abolish the epithelial expression is also unknown. Based on the limited

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teaching of the specification, the description of the core structure of the claimed promoter is not sufficient for supporting the claimed genus of nucleic acids, especially the functional equivalents as recited in claim 1. Therefore, the written description rejection is maintained.

In response to the new matter rejection directed to claim 14, Applicants argue that the specification provides support by stating that “expression of a nucleic acid of interest operably linked to a promoter or a functional fragment thereof as provided by the invention is thus mainly restricted to normal adult non-squamous epithelium or neoplasias derived from epithelia...” and “carcinomas, in general are the malignant counter parts or neoplasia derived from epithelia.”

This argument is not found persuasive. As discussed in previous office action, claim 14 is directed to a medicament for treating epithelial cancer comprising an isolated or recombinant nucleic acid sequence according to claim 1. The above quoted statements do not describe such a medicament because the first statement describes tissue specific expression of the promoter activity, and the later describes different kinds of carcinoma. Neither such description is directed to a medicament as claimed. Therefore, the new matter rejection is maintained.

Claim 14 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the specification provides an animal model that phenotypically correlates to epithelial cancer. Applicants assert this model has great

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significance because the mechanisms that regulate immunological tolerance to tumor antigens are formidable obstacles that withstand effective tumor immunotherapy in cancer patients.

Applicants further assert that EGF-2 is one of the best-studied tumor associated antigens frequently used as an attractive target for experimental and clinical cancer therapy. Moreover, Applicants state that the state of art and the instant specification reflect the fact that suicide genes and their prodrugs are well known, and the claimed promoter has epithelial specific activity such that suicide genes may be expressed specifically in epithelial tissue. Applicants conclude that the claimed invention is enabled based on such teachings.

The argument has been considered but deemed unpersuasive. As discussed in the previous action, the state of art regard gene therapy as unpredictable. The success of certain prodrug is based on trial and error, not routine experimentation. The instant claim is drawn to a medicament comprising an epithelial specific promoter that is able to direct expression of suicide gene. The instant specification does not teach or give a working example of such medicament that is able to treat epithelial cancer. The presence of a transgenic mouse model of human disease may be useful for screening compounds that can potentially treat human epithelial cancer, however, it is not a teaching of a medicament. Based on the limited teaching of the instant specification and the art-recognized unpredictability, the claimed medicament is not enabled. Therefore, this rejection is maintained.

### ***Conclusion***

No claims are allowed.

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

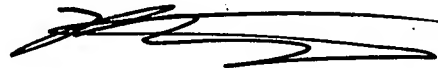
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.  
Examiner  
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CELINE QIAN, PH.D.  
PRIMARY EXAMINER

A handwritten signature in dark ink, appearing to be 'C. Qian', written over a horizontal line.